

WHAT IS CLAIMED IS:

1 1. An anti-mesothelin antibody which binds to recombinant mesothelin
2 with a dissociation constant of less than 3×10^{-8} M and specifically binds to cells expressing
3 mesothelin on their cell surface.

1 2. The antibody of claim 1, wherein the CDRs of said antibody are as
2 indicated in SEQ ID NO:5.

1 3. The antibody of claim 1, comprising a single chain Fv antibody
2 comprising a variable heavy (V_H) region and a variable light (V_L) region.

1 4. The antibody of claim 3, wherein said V_L is conjugated to said V_H
2 through a linker peptide.

1 5. The antibody of claim 3, wherein said antibody is a dsFv.

1 6. The antibody of claim 3, wherein the variable heavy (V_H) region is
2 encoded by SEQ ID NO:1.

1 7. The antibody of claim 3, wherein the variable light (V_L) region is
2 encoded by SEQ ID NO:1.

1 8. The antibody of claim 3, wherein said single chain Fv antibody
2 comprises a variable heavy (V_H) region and a variable light (V_L) region encoded by SEQ ID
3 NO:1.

1 9. The antibody of claim 1, wherein said antibody is detectably labeled.

1 10. The antibody of claim 1, wherein said antibody is conjugated to an
2 therapeutic agent.

- 1 11. The antibody of claim 10, wherein said therapeutic agent is a toxin.
- 1 12. The antibody of claim 11, wherein said toxin is a *Pseudomonas*
2 exotoxin (PE) or cytotoxic fragment thereof.
- 1 13. An anti-mesothelin antibody wherein the variable heavy (V_H) region is
2 as shown in SEQ ID NO:5.
- 1 14. An anti-mesothelin antibody wherein the variable light (V_L) region is
2 as shown in SEQ ID NO:5.
- 1 15. An anti-mesothelin antibody wherein the CDRs are as shown in SEQ
2 ID NO:5.
- 1 16. An anti-mesothelin antibody wherein said antibody comprises a
2 variable heavy (V_H) region and a variable light (V_L) region of SEQ ID NO:5.
- 1 17. The antibody of claim 16, wherein said antibody is a scFv.
- 1 18. An anti-mesothelin antibody, said antibody produced by a process
2 comprising of the steps:
3 (i) immunizing a mammal with an expression cassette which
4 comprises cDNA encoding mammalian mesothelin;
5 (ii) removing the spleen from said mammal;
6 (iii) preparing a phage display library from said spleen of said
7 animal;
8 (iv) selecting for a phage which displays an antibody which binds to
9 recombinant mesothelin with a dissociation constant of less than 3×10^{-8} M and specifically
10 binds to cells expressing mesothelin on their cell surface;

- 11 (v) isolating the nucleic acid sequence which encodes said
12 antibody;
13 (vi) introducing said nucleic acid sequence into a cell such that said
14 antibody is expressed by said cell; and
15 (vii) isolating said antibody from said cell.

1 19. The antibody of claim 18, further comprising recombinantly fusing in
2 frame said nucleic acid sequence with a nucleic acid sequence which encodes a *Pseudomonas*
3 exotoxin or cytotoxic fragment thereof.

1 20. A recombinant immunoconjugate, comprising a therapeutic agent or a
2 detectable label bonded to an anti-mesothelin antibody which binds to recombinant
3 mesothelin with a dissociation constant of less than 3×10^{-8} M and specifically binds to cells
4 expressing mesothelin on their cell surface.

1 21. The immunoconjugate of claim 20, wherein CDRs of said antibody are
2 as indicated in SEQ ID NO:5.

1 22. The immunoconjugate of claim 20, comprising a single chain Fv
2 antibody comprising a variable heavy (V_H) region and a variable light (V_L) region.

1 23. The immunoconjugate of claim 22, wherein said V_H region is peptide
2 bonded to said V_L region through a linker peptide.

1 24. The immunoconjugate of claim 22, wherein the variable heavy (V_H)
2 region is encoded by SEQ ID NO:1.

1 25. The immunoconjugate of claim 22, wherein the variable light (V_L)
2 region is encoded by SEQ ID NO:1.

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1 26. The immunoconjugate of claim 22, wherein said single chain Fv
2 antibody comprises a variable heavy (V_H) region and a variable light (V_L) region of SEQ ID
3 NO:1.

1 27. The immunoconjugate of claim 20, wherein said antibody is
2 conjugated to a therapeutic agent.

1 28. The immunoconjugate of claim 27, wherein said therapeutic agent is a
2 toxin.

1 29. The immunoconjugate of claim 28, wherein said toxin is a
2 *Pseudomonas* exotoxin (PE) or cytotoxic fragment thereof.

1 30. The immunoconjugate of claim 29, wherein said cytotoxic fragment is
2 PE38.

1 31. The immunoconjugate of claim 20, wherein said variable heavy (V_H)
2 region is peptide bonded to the therapeutic agent or detectable label.

1 32. The immunoconjugate of claim 20, wherein said immunoconjugate is
2 encoded by SEQ ID NO:2.

1 33. An expression cassette encoding said antibody of claim 3.

1 34. The expression cassette of claim 33, wherein the CDRs of said
2 antibody are as indicated in SEQ ID NO:5.

1 35. The expression cassette of claim 33, comprising a single chain Fv
2 antibody comprising a variable heavy (V_H) region and a variable light (V_L) region.

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1 36. The expression cassette of claim 35, wherein V_H region is peptide
2 bonded to said V_L region through a linker peptide.

1 37. The expression cassette of claim 35, wherein the variable heavy (V_H)
2 region is encoded by SEQ ID NO:1.

1 38. The expression cassette of claim 35, wherein the variable light (V_L)
2 region is encoded by SEQ ID NO:1.

1 39. The expression cassette of claim 35, wherein said single chain Fv
2 antibody comprises a variable heavy (V_H) region and a variable light (V_L) region of SEQ ID
3 NO:1.

1 40. The expression cassette of claim 33, wherein said antibody is
2 detectably labeled.

1 41. The expression cassette of claim 33, wherein said antibody is
2 conjugated to a therapeutic agent.

1 42. The expression cassette of claim 41, wherein said therapeutic agent is a
2 toxin.

1 43. The expression cassette of claim 42, wherein said toxin is a
2 *Pseudomonas* exotoxin (PE) or cytotoxic fragment thereof.

1 44. An expression cassette encoding said recombinant immunoconjugate
2 of claim 22.

1 45. The expression cassette of claim 44, wherein CDRs of said antibody
2 are as indicated in SEQ ID NO:5.

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1 46. The expression cassette of claim 44, wherein said antibody is a single
2 chain antibody comprising of a variable heavy (V_H) region and a variable light (V_L) region.

1 47. The expression cassette of claim 46, wherein said V_H region is peptide
2 bonded to said V_L region through a linker peptide.

1 48. The expression cassette of claim 46, wherein the variable heavy (V_H)
2 region is encoded by SEQ ID NO:1.

1 49. The expression cassette of claim 46, wherein the variable light (V_L)
2 region is encoded by SEQ ID NO:1.

1 50. The expression cassette of claim 46, wherein said single chain antibody
2 comprises a variable heavy (V_H) region and a variable light (V_L) region of SEQ ID NO:1.

1 51. The expression cassette of claim 44, wherein said therapeutic agent is a
2 toxin.

1 52. The expression cassette of claim 51, wherein said toxin is a
2 *Pseudomonas* exotoxin (PE) or a cytotoxic fragment thereof.

1 53. The expression cassette of claim 52, wherein said cytotoxic fragment is
2 PE38.

1 54. The expression cassette of claim 52, wherein a variable heavy region is
2 peptide bonded to the *Pseudomonas* exotoxin (PE) or cytotoxic fragment thereof.

1 55. A host cell comprising said expression cassette of claim 33.

1 56. The host cell of claim 55, wherein the CDRs of said antibody are as
2 indicated in SEQ ID NO:5.

1 57. The host cell of claim 55, comprising a single chain Fv antibody
2 comprising a variable heavy (V_H) region and a variable light (V_L) region.

1 58. The host cell of claim 57, wherein said V_H region is peptide bonded to
2 said V_L region through a linker peptide.

1 59. The host cell of claim 57, wherein the variable heavy (V_H) region is
2 encoded by SEQ ID NO:1.

1 60. The host cell of claim 57, wherein the variable light (V_L) region is
2 encoded by SEQ ID NO:1.

1 61. The host cell of claim 57, wherein said single chain Fv antibody
2 comprises a variable heavy (V_H) region and a variable light (V_L) region of SEQ ID NO:1.

1 62. The host cell of claim 55, wherein said antibody is detectably labeled.

1 63. The host cell of claim 55, wherein said antibody is conjugated to a
2 therapeutic agent.

1 64. The host cell of claim 63, wherein said therapeutic agent is a toxin.

1 65. The host cell of claim 64, wherein said toxin is a *Pseudomonas*
2 exotoxin (PE) or cytotoxic fragment thereof.

1 66. A host cell comprising said expression cassette of claim 44.

1 67. The host cell of claim 66, wherein CDRs of said antibody are as
2 indicated in SEQ ID NO:5.

1 68. The host cell of claim 66, wherein said antibody is a single chain
2 antibody comprising of a variable heavy (V_H) region and a variable light (V_L) region.

1 69. The host cell of claim 57, wherein said V_H region is peptide bonded to
2 said V_L region through a linker peptide.

1 70. The host cell of claim 57, wherein the variable heavy (V_H) region is
2 encoded by SEQ ID NO:1.

1 71. The host cell of claim 57, wherein the variable light (V_L) region is
2 encoded by SEQ ID NO:1.

1 72. The host cell of claim 57, wherein said single chain antibody
2 comprises a variable heavy (V_H) region and a variable light (V_L) region of SEQ ID NO:1.

1 73. The host cell of claim 63, wherein said therapeutic agent is a toxin.

1 74. The host cell of claim 73, wherein said toxin is a *Pseudomonas*
2 exotoxin (PE) or a cytotoxic fragment thereof.

1 75. The host cell of claim 74, wherein said PE is PE38.

1 76. A method for inhibiting the growth of a malignant cell expressing
2 mesothelin on its cell surface, said method comprising:
3 contacting said malignant mesothelial cell with an effective amount of an
4 immunoconjugate comprising a toxin peptide bonded to an anti-mesothelin antibody which
5 binds to recombinant mesothelin with a dissociation constant of less than 3×10^{-8} M and
6 specifically binds to cells expressing mesothelin on their cell surface.

1 77. The method of claim 76, wherein said antibody comprises CDRs as
2 indicated in SEQ ID NO:5.

1 78. The method of claim 76, wherein said anti-mesothelin antibody is a
2 single chain Fv antibody comprising a variable heavy (V_H) region and a variable light (V_L)
3 region.

1 79. The method of claim 78, wherein said V_H region is peptide bonded to
2 said V_L region through a linker peptide.

1 80. The method of claim 78, wherein the variable heavy (V_H) region is
2 encoded by SEQ ID NO:1.

1 81. The method of claim 78, wherein the variable light (V_L) region is
2 encoded by SEQ ID NO:1.

1 82. The method of claim 78, wherein said scFv fragment comprises a
2 variable heavy (V_H) region and a variable light (V_L) region of SEQ ID NO:1.

1 83. The method of claim 76, wherein said toxin is a *Pseudomonas*
2 exotoxin (PE) or a cytotoxic fragment thereof.

1 84. The method of claim 83, wherein said PE is PE38.

1 85. The method of claim 83, wherein a variable heavy region is peptide
2 bonded to the toxin.

1 86. The method of claim 76, wherein said malignant cell is contacted *in*
2 *vivo*.

1 87. The method of claim 76, wherein said malignant cell is selected from
2 the group malignancies consisting of mesotheliomas, ovarian cancer, stomach cancer and
3 squamous cell cancer.

1 88. A method for detecting the presence of mesothelin in a biological
2 sample, said method comprising:

3 (i) contacting said biological sample with an anti-mesothelin
4 antibody which binds to recombinant mesothelin with a dissociation constant of less than $3 \times$
5 10^{-8} M and specifically binds to cells expressing mesothelin on their cell surface;

6 (ii) allowing said antibody to bind to mesothelin under
7 immunologically reactive conditions, wherein detection of said bound antibody indicates the
8 presence of said mesothelin.

1 89. The method of claim 88, wherein said antibody comprises CDRs as
2 indicated in SEQ ID NO:5.

1 90. The method of claim 88, wherein said anti-mesothelin antibody is a
2 single chain Fv antibody comprising a variable heavy (V_H) region and a variable light (V_L)
3 region.

1 91. The method of claim 90, wherein said V_H region is peptide bonded to
2 said V_L region through a linker peptide.

1 92. The method of claim 90, wherein the variable heavy (V_H) region is
2 encoded by SEQ ID NO:1.

1 93. The method of claim 90, wherein the variable light (V_L) region is
2 encoded by SEQ ID NO:1.

1 94. The method of claim 90, wherein said scFv fragment comprises a
2 variable heavy (V_H) region and a variable light (V_L) region of SEQ ID NO:1.

1 95. The method of claim 88, wherein said antibody is detectably labeled.

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96. The method of claim 88, wherein the method is performed *in vivo* in a mammal.

97. A pharmaceutical composition comprising the immunoconjugate of claim 20.

98. A kit for detecting mesothelin on the surface of cells, said kit comprising:

- (i) an anti-mesothelin antibody which binds to recombinant mesothelin with a dissociation constant of less than 3×10^{-8} M and specifically binds to cells expressing mesothelin on their cell surface; and
- (ii) instructions printed on a tangible medium, said instructions describing the methods of using and uses for said antibody.

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